REMARKS

Applicant has canceled claims 2, 22 and 32 without prejudice or disclaimer of the subject matter recited therein, and expressly reserves all rights to such subject matter. Applicant proposes to amend claims 1, 3, 21, 23, 31 and 33, and proposes to add new claims 42 and 43. A marked-up copy of the amended claims is attached. Upon entry of this amendment, claims 1, 3-8, 21, 23-31 and 33-43 will be pending. Applicants submit that addition of claims is appropriate after final rejection because the total number of claims pending after this amendment will be less than the total number of claims pending prior to this amendment.

Applicant appreciates that most of the previous rejections have been withdrawn. Without acquiescing in the remaining rejections, applicant amended claims to make the steps more consonant with the preamble. Applicant also has clarified an issue raised by the examiner regarding "determining" in claim 2. Applicant has combined claim 2 with claim 3 and made the recitation apply to "all" determining. Similar changes were made to claims 23 and 33.

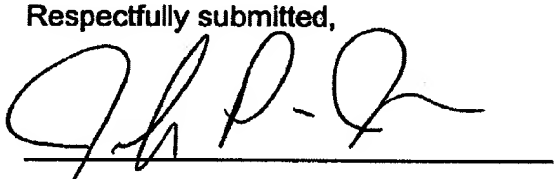
Applicant notes the examiner's discussion of the invention in relation to claims 1 and 21. Applicant's use of nucleic acids (or "NAs" as termed by the examiner) refers to a plurality of nucleotides bound by covalent linkages such that there is a sequence, as opposed to mere nucleotides in solution. Thus, when the nuclease is added to a sample, free (unencapsulated) "nucleic acids" are digested, which leaves only the encapsulated nucleic acids in a sequence form. The amount of encapsulated nucleic acids in the sample can then be determined, and the amount of free nucleic acids can

be determined by subtracting the amount of encapsulated nucleic acids from the overall amount of nucleic acids in the sample originally (determined prior to nuclease treatment).

Request

Applicants submit that the claims are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 912-2000 should there be any questions.

Respectfully submitted,



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Marked-up Copy of Amended Claims

1. (Twice amended) A method for determining the type of target nucleic acids in a sample, wherein the method is capable of differentiating free and encapsulated target nucleic acids in the sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest free target nucleic acids in the sample to form a **[digested]** **nuclease-treated** sample;

(c) determining a total target nucleic acid content remaining in the **[digested]** **nuclease-treated** sample**, thereby quantifying the amount of encapsulated target nucleic acids in the sample**; and

(d) quantifying the total amount of free target nucleic acid in the sample by subtracting the determined amount of target nucleic acid content in the **[digested]** **nuclease-treated** sample from the determined amount of total target nucleic acid content in the sample**, wherein steps (c) and (d) determine the types of target nucleic acids in the sample**.

3. (Twice amended) The method of claim **[2]** 1, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay selected from the group consisting of** **[the nucleic acid amplification assay is]** a polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

21. (Amended) A method for determining the proportion**[s]** of infectious pathogens and inactivated pathogens in a sample, wherein the method is capable of differentiating free and encapsulated target nucleic acids in the sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest free target nucleic acids in the sample to form a **[digested]** **nuclease-treated**, wherein the nuclease will not digest the encapsulated target nucleic acids;

(c) determining a total target nucleic acid content remaining **undigested** in the **[digested]** **nuclease-treated** sample, which represents the amount of infectious pathogens in the sample;

(d) quantifying the total amount of free target nucleic acid in the sample by subtracting the determined amount of **undigested** target nucleic acid content in the **[digested]** **nuclease-treated** sample from the determined amount of total target nucleic acid content in the sample, wherein the quantifying indicates the amount of inactivated pathogens in the sample**; and**

(e) comparing the amounts from steps (c) and (d) to determine the proportion of infectious pathogens and inactivated pathogens in the sample.

23. (Amended) The method of claim **[22]** **21**, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay select d from th gr up c nsisting of** **[th nucl ic acid amplification assay is]** a

polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

31. (Amended) A method for detecting infectious pathogens in a sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest any free target nucleic acids in the sample to form a **[digested]** **nuclease-treated** sample, wherein the nuclease will not digest the encapsulated target nucleic acids; and

(c) **detecting infectious pathogens that may be present in the sample by** determining a total target nucleic acid content remaining in the **[digested]** **nuclease-treated** sample, which represents the amount of infectious pathogens in the sample.

33. (Amended) The method of claim **[32]** **31**, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay selected from the group consisting of** **[the nucleic acid amplification assay is]** a polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

Marked-up Copy of Amended Claims

1. (Twice amended) A method for determining the type of target nucleic acids in a sample, wherein the method is capable of differentiating free and encapsulated target nucleic acids in the sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest free target nucleic acids in the sample to form a **[digested]** **nuclease-treated** sample;

(c) determining a total target nucleic acid content remaining in the **[digested]** **nuclease-treated** sample**, thereby quantifying the amount of encapsulated target nucleic acids in the sample**; and

(d) quantifying the total amount of free target nucleic acid in the sample by subtracting the determined amount of target nucleic acid content in the **[digested]** **nuclease-treated** sample from the determined amount of total target nucleic acid content in the sample**, wherein steps (c) and (d) determine the types of target nucleic acids in the sample**.

2 ~~3.~~ (Twice amended) The method of claim **[2]** 1, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay selected from the group consisting of** **[the nucleic acid amplification assay is]** a polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

3 ~~4.~~ (Amended) The method of claim 1, further comprising adding **a** nucleic acid standard to **[said] the** sample before **[said] the [first]** total target nucleic acid content **of (a)** is determined.

4 ~~5.~~ (Amended) The method of claim 1, further comprising adding **a** nucleic acid standard to **[said] the** sample after **the** free target nucleic acid**s** in **[said] the** sample are digested with **[said] the** nuclease.

5 ~~6.~~ (Amended) The method of claim 1, wherein **[said] the** nuclease is inactivated after **[said] the** free nucleic acids in **[said] the** sample are digested.

6 ~~7.~~ (Amended) The method of claim 1, wherein **[said] the** nuclease is **a** DNase or **an** RNase.

7 ~~8.~~ (Amended) The method of claim 1, wherein **[said] the** sample is selected from the group consisting of blood, plasma, serum, cell culture fluids, cells and a pharmaceutical preparation.

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21. (Amended) A method for determining the proportion**[s]** of infectious pathogens and inactivated pathogens in a sample, wherein the method is capable of differentiating free and encapsulated target nucleic acids in the sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest free target nucleic acids in the sample to form a **[digested]** **nuclease-treated**, wherein the nuclease will not digest the encapsulated target nucleic acids;

(c) determining a total target nucleic acid content remaining **undigested** in the **[digested]** **nuclease-treated** sample, which represents the amount of infectious pathogens in the sample;

(d) quantifying the total amount of free target nucleic acid in the sample by subtracting the determined amount of **undigested** target nucleic acid content in the **[digested]** **nuclease-treated** sample from the determined amount of total target nucleic acid content in the sample, wherein the quantifying indicates the amount of inactivated pathogens in the sample**; and**

(e) comparing the amounts from steps (c) and (d) to determine the proportion of infectious pathogens and inactivated pathogens in the sample.

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23. (Amended) The method of claim **[22]** 21, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay selected from the group c nsi ting of [th nucl ic acid amplificati n assay is]** a

polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

31. (Amended) A method for detecting infectious pathogens in a sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest any free target nucleic acids in the sample to form a **[digested]** **nuclease-treated** sample, wherein the nuclease will not digest the encapsulated target nucleic acids; and

(c) **detecting infectious pathogens that may be present in the sample by** determining a total target nucleic acid content remaining in the **[digested]** **nuclease-treated** sample, which represents the amount of infectious pathogens in the sample.

33. (Amended) The method of claim **[32]** **31**, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay selected from the group consisting of** **[the nucleic acid amplification assay is]** a polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

from the determined amount of total target nucleic acid content in the sample, wherein the quantifying indicates the amount of inactivated pathogens in the sample.

22. (New) The method of claim 21, wherein the determining of the target nucleic acids is performed using a nucleic acid amplification assay.

23. (New) The method of claim 22, wherein the nucleic acid amplification assay is a polymerase chain reaction (PCR) assay or a reverse transcriptase (RT) PCR assay.

24. (New) The method of claim 21, further comprising adding a nucleic acid standard to the sample before the total target nucleic acid content of (a) is determined.

25. (New) The method of claim 21, further comprising adding a nucleic acid standard to the sample after the free target nucleic acids in the sample are digested with the nuclease.

26. (New) The method of claim 21, wherein the nuclease is inactivated after the free nucleic acids in the sample are digested.

27. (New) The method of claim 21, wherein the nuclease is a DNase or an RNase.

28. (New) The method of claim 21, wherein the sample is selected from the group consisting of blood, plasma, serum, cell culture fluids, cells and a pharmaceutical preparation.

29. (New) The method according to claim 21, wherein the pathogen is a virus.

30. (New) The method according to claim 29, wherein the virus is selected from the group consisting of parvovirus, hepatitis virus and human immunodeficiency virus.

31. (New) A method for detecting infectious pathogens in a sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest any free target nucleic acids in the sample to form a digested sample, wherein the nuclease will not digest the encapsulated target nucleic acids; and

(c) determining a total target nucleic acid content remaining in the digested sample, which represents the amount of infectious pathogens in the sample.

32. (New) The method of claim 31, wherein the determining of the target nucleic acids is performed using a nucleic acid amplification assay.

polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

17 ~~31.~~ (Amended) A method for detecting infectious pathogens in a sample, wherein the method comprises

(a) determining a total target nucleic acid content in the sample;

(b) adding a nuclease to the sample to digest any free target nucleic acids in the sample to form a **[digested]** **nuclease-treated** sample, wherein the nuclease will not digest the encapsulated target nucleic acids; and

(c) **detecting infectious pathogens that may be present in the sample by** determining a total target nucleic acid content remaining in the **[digested]** **nuclease-treated** sample, which represents the amount of infectious pathogens in the sample.

18 ~~33.~~ (Amended) The method of claim **[32]** ~~31~~ 17, wherein **all determining of the target nucleic acids is performed using a nucleic acid amplification assay selected from the group consisting of** **[the nucleic acid amplification assay is]** a polymerase chain reaction (PCR) assay **[or]** **and** a reverse transcriptase (RT) PCR assay.

33. (New) The method of claim 32, wherein the nucleic acid amplification assay is a polymerase chain reaction (PCR) assay or a reverse transcriptase (RT) PCR assay.

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34. (New) The method of claim 31, further comprising adding a nucleic acid standard to the sample before the total target nucleic acid content of (a) is determined.

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35. (New) The method of claim 31, further comprising adding a nucleic acid standard to the sample after the free target nucleic acids in the sample are digested with the nuclease.

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36. (New) The method of claim 31, wherein the nuclease is inactivated after the free nucleic acids in the sample are digested.

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37. (New) The method of claim 31, wherein the nuclease is a DNase or an RNase.

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39. (New) The method of claim 31, wherein the sample is selected from the group consisting of blood, plasma, serum, cell culture fluids, cells and a pharmaceutical preparation.

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40. (New) The method according to claim 31, wherein the pathogen is a virus.

41. (New) The method according to claim 40, wherein the virus is selected from the group consisting of parvovirus, hepatitis virus and human immunodeficiency virus.